

UNIVERSITY OF ZAMBIA

SCHOOL OF MEDICINE

**MALIGNANT BREAST DISEASE AT THE UNIVERSITY
TEACHING HOSPITAL – FREQUENCY OF KNOWN RISK
FACTORS AND PRESENTATION**

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Thesis
(M.Med.)

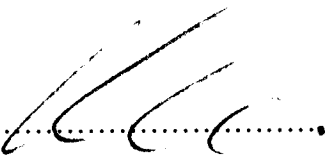
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CERTIFICATION

This is to certify that this dissertation authored by Bruce C. Bvulani is ready for examination
for the award of the Master of Medicine (Surgery) degree by the University of Zambia.

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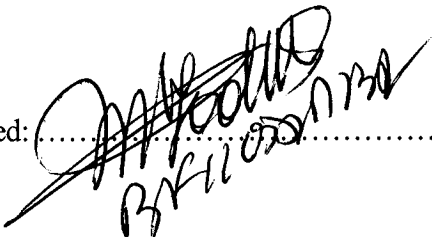

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APPROVAL

This dissertation by Bruce C. Bvulani has been approved as fulfilling part of the requirements for the award of the Master of Medicine Degree (Surgery) by the University of Zambia.

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Signed:  Date : 6/05/06

DEDICATION

To my Creator, God, and to my wife, Margaret and all the vulnerable women who are at risk of suffering from breast cancer at some stage in their short life on earth.

ACKNOWLEDGEMENT

Firstly, I am greatly indebted to my supervisor, Prof Krikor Erzingatsian, and my co-supervisor, Mr Kasonde Bowa, for their expert guidance and support, without which this document would have been incomplete.

Special thank you to Dr Yotham Phiri and his wife for the help rendered during the typing and typesetting of this document.

Finally, I wish to acknowledge all the patients who participated in the study for their willingness and support.

DECLARATION

I hereby declare that the work presented in this study for the degree of Master of Medicine (Surgery) has not been presented in the past or currently either wholly or in part for any other degree.

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Student

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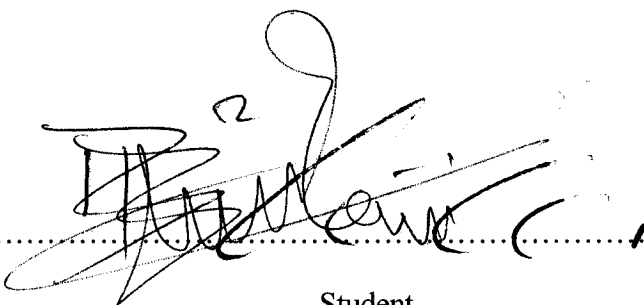
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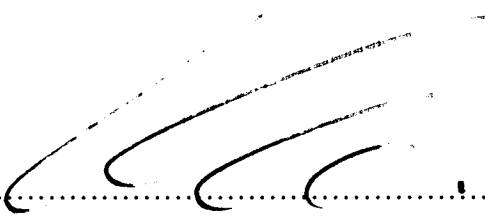
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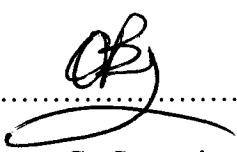
I hereby declare that the work presented in this study for the degree of Master of Medicine (Surgery) has not been presented in the past or currently either wholly or in part for any other degree.

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SUMMARY

A prospective uncontrolled observational study was undertaken to assess the risk factors and the frequency of known presenting symptoms in women attending the Surgery department of the University Teaching Hospital, over an eight-month period. Breast cancer is a major problem affecting women in Zambia and a study to highlight risk factors and the common presenting symptoms was deemed necessary. Patients admitted to the general surgical wards and those attending the tumour clinic were interviewed, examined and biopsy results collected. The socio-economical background, obstetrical and other information of the patients was compared with that known of the general female population.

Thirty-seven patients were included in the study. Their mean age was 48.6 years, half being postmenopausal. The patients were of a low socio-economical background and enjoying a predominantly vegetable based diet as in the general Zambian population. They drank alcohol and used hormonal contraceptives more than the rest of the population. Hence probable risk factors for breast cancer for this study group were a positive family history, an increased alcohol consumption and contraceptive use. Breastfeeding and increased parity, similar to that of the general population, did not seem to confer protection against development of breast.

Patients reported upon discovering a lump by themselves and in most instances presented late. The tumours were characteristically large and commonly presenting with axillary lymphadenopathy as reported elsewhere in the literature.

This study illustrates the need for better education for both the vulnerable women of Zambia and the primary health care personnel in contact with them so that early diagnosis can be made and timely intervention undertaken. It can form the basis for a larger multi-centre prospective study to investigate breast cancer in Zambia and the region.

INTRODUCTION

Malignant breast disease is a major problem the world over and a leading cause of mortality among females¹⁻⁴. The incidence of breast cancer in the Western hemisphere is on the increase, affecting women over 45 years of age (only 2% below 30 years of age are affected)^{2,3,5}. Observations made in Africa suggest the disease is more aggressive and affects a younger age group⁶⁻⁸. There is a similar trend seen in Lusaka and the Zambian population⁹.

Risk factors for breast cancer worldwide are many but the greatest risk is in people with a positive family history^{2,4,10}. Other factors considered include social class, geographical location, diet, obesity, contraceptive use and oestrogen hormone therapy. Studies done in Africa show a higher prevalence in Caucasians compared to the Negro population¹¹.

The various factors stated need to be explored in our Zambian context. An assessment of the following factors is to be done:

- (i) areas of the country most affected
- (ii) what dietary factors if any may be contributory
- (iii) social/lifestyle factors (alcohol consumption /smoking)
- (iv) birthing and birth control habits.

Studies to look at the frequency of known risk factors in Africa as a whole, and the east and south African sub-region have been done^{7,12-14}. The common presentation is of a mass in the breast with or without pain and fungation in the more advanced stages. Unlike in the Western hemisphere the majority of patients present with stage III and IV disease^{11,12,15}. In the developed world patients present early²⁻⁴.

Thus clinical presentation and history of the presentation need to be assessed. This would aid in putting measures in place for early diagnosis and treatment.

STATEMENT OF THE PROBLEM

Worldwide up to 10 % of all women at some stage during life will develop breast cancer^{2, 4,8,10}. There is much written in the regional literature on the subject of breast cancer, however, no studies in Zambia on risk factors or the frequency of known clinical presentations has been done. Breast cancer is a major problem in the Zambian female population but the male is rarely affected in this population as noted elsewhere^{10,14}.

Estimates done in Zambia rank breast cancer as a leading cause of cancer deaths. Studies are needed that can indicate possible causal and risk factors associated with malignant breast disease and the common clinical presentation as seen in Zambia. Such studies could help authorities to plan means of managing this major burden on health resources and perhaps introduce health education measures to deal with the problem.

Presently, women in Zambia and elsewhere in the region are known to present late to health institutions and thus have a poorer prognosis. If the common presentations in our environment were known then perhaps women would be taught about breast awareness and specifically what to look out for as early signs of the disease.

LITERATURE REVIEW

RISK FACTORS FOR BREAST CANCER: -

Various factors such as diet, race, geographical location, hormonal changes and family history are said to have a role in the aetiology of breast cancer. Despite the recognition of these risk factors up to 70% of people have no recognised risk factors^{5,10}. Some of the most important risk factors are elaborated here.

FAMILY HISTORY²

A positive family history and genetic predisposition increase the risk of breast cancer. A history of carcinoma in the mother, daughter or sibling increases the risk substantially and the risk falls with more distant relatives. Risk is much higher if the affected first-degree relative had pre menopausal or bilateral breast cancer^{2,4,8,16}.

It has been shown that a family history is the most important factor in breast cancer development^{2,5}. Up to 10% have genetically related breast cancer^{8,13,17}. In 1994, mutations of either the BRCA1 gene on the long arm of chromosome 17 or BRCA 2 on chromosome 13 were noted to be the cause of most hereditary breast cancer. Seventy other genes were associated. The BRCA1 and BRCA 2 genes conferred different histological characteristics to breast carcinoma. On the basis of this work, BRCA 1 tumours are said to be less hormone receptor positive than BRCA 2 tumours and thus BRCA 1 tumours are less responsive to treatment with antioestrogen therapy^{2-4,18}.

AGE/MENARCHE:-

Age of itself is not thought to be a significant factor but age at menarche and establishment of regular ovulatory cycles seem to be strongly associated with breast cancer risk. A delayed menarche is said to reduce the risk of breast cancer while early menopause before 45 years has been shown to reduce the risk possibly because of reduced oestrogen levels at an earlier age^{3,4}. Also early oophorectomy below 50 years has been shown to reduce the risk. Thus a reduced menstrual life reduces the risk of breast cancer¹⁰. In an East African study delayed menarche was associated with increased risk and this seemed to contradict these findings¹⁹.

PARITY/AGE AT FIRST PREGNANCY:-

Nulliparous women are at greater risk of developing breast cancer than parous women. It has become increasingly apparent that the effect of pregnancy on breast cancer risk varies with the age at first birth. Further more, with women whose first pregnancy occurs after 30 have a two to fivefold increase in risk compared with women having a first pregnancy before age 18 or 19^{4,5,10,15}. This is consistent with studies done in Africa^{15,19}.

HORMONAL FACTORS :-

As already noted breast cancer in the Occident has been shown to affect more peri and postmenopausal age groups and rarely women below 30 years of age^{2,10}. Hormonal changes in the body have been thought to play a part in the development of breast cancer. A well-established form of therapy advocates the use of tamoxifen, an antioestrogen hormone to suppress breast malignancy^{2,20}.

High prolactin levels in postmenopausal women have been shown to increase the risk of breast cancer but this has not been proven conclusively. Such hormones are currently under study^{21,22,23}.

There has been evidence to suggest that long term use of oestrogen contraceptive use and hormone replacement therapy increase the risk in premenopausal women^{10,24,25,26}. Some have suggested that the risk is more before the first child is born. It has also been shown that termination of pregnancy has a role as well. This is thought to be due to abrupt changes in oestrogen hormone levels and is said to be only associated with benign breast disease²³. Other studies show that there is no connection between breast cancer and oestrogen hormone use²⁶.

LACTATION :-

Studies in Japan, in Uganda and elsewhere have showed that lactation confers a protective effect against breast cancer development^{11,19,27}. Newcomb and colleagues showed that this

is only significant within the pre-menopausal age group²². With an increasing cumulative duration of lactation, there was a decreasing risk of breast cancer among pre-menopausal women¹⁰. In the ongoing US nurses health study no significant association between breast cancer and cumulative breastfeeding was noted in 89,887 subjects followed up²⁸.

RACE AND GEOGRAPHIC LOCATION:-

In the Japanese female population and in observations made in Europe, geographic location has been thought to be a factor in breast cancer aetiology^{11,27}. Recent intercontinental movements and lifestyle changes suggest that other factors such as diet and environment may have a bigger role to play than race^{10,17}. For instance, there are more Japanese women with breast cancer in Japan today than ever before and Japanese women living in the U.S.A have similar rates of disease as the indigenous Americans³.

Studies done in Africa^{6,17,19} showed that Caucasians were affected more often than the Negro population but the duration of the disease in white women living in Europe took a longer course with a better prognosis compared to African women. Initially, this was thought to be due to late presentation in African patients⁶ or the disease could have been more aggressive due to factors yet to be determined. Hassan suggested that the survival disadvantage is probably the result of a combined effect of delayed presentation by the patient, the preponderance of biologically very aggressive tumours and our grossly limited therapeutic modalities¹³. Others are of the opinion that late presenting tumours had better prognosis²⁹.

SOCIAL LIFESTYLE: -

Alcohol intake and cigarette smoking in one African study did not seem to show an increase in the risk of developing breast carcinoma¹¹. Several studies in the western world have shown that there is an increased risk in both alcoholics and smokers^{10,24,30,31}. Most studies show an increased risk with moderate alcohol consumption but smoking has been found to be unimportant in the causation of breast cancer^{4,24,30}.

DIET/OBESITY :-

Currently there is conclusive evidence that dietary fat intake significantly increases risk of breast carcinoma or that a reduction in fat intake improves prognosis of already diagnosed cancer^{10,32}. Thus, there is an increased incidence of breast cancer and other cancers for that matter among obese and overweight women. In studies done in Africa there has been no significant relationship between diet and breast cancer perhaps because the diet is not predominantly fat based^{6,11,15}. Dietary fiber intake has been suggested to confer a protective role in the development of cancer of the breast specifically and of other cancers³. One study noted an increased risk with high starch intakes which is predominant in our environment³³.

SOCIAL ECONOMIC STATUS: -

Some studies done in Europe and elsewhere have shown that low income groups are more commonly affected^{7,19,23,33}. Many dispute this and have shown that the more affluent are at greater risk^{24,30}. It has also been shown that women of poorer communities tend to have more aggressive high grade tumours³⁴. Some studies have shown that increased risk was found to be associated with stressful life events, which perhaps may be significant in our setting where our women are forever worried about their next meal³⁹.

RADIATION: -

Epidemiological studies have shown that women exposed to ionizing radiation due to nuclear war or medical diagnostic and therapeutic procedures are at increased risk for the development of breast cancer. The risk is less in women greater than 40 years of age^{11,30}.

ATYPICAL HYPERPLASIA :-

There is an increased risk of breast cancer after 10 years, if a biopsy done for proliferative breast disease shows atypical hyperplasia on histology or in patients showing non invasive intraductal or lobular carcinoma-in situ^{2,10,24}.

CLINICAL PRESENTATION OF PATIENTS:

The commonest symptom seen in patients is a mass discovered by the patient or the physician ^{5,6}. About 90% of breast cancer is discovered by the patient. The lump may be painful and increasing in size rapidly or painless and with or without skin changes and ulceration. There may be associated nipple discharge as well. The other presentation commonly seen is the involvement of regional lymph nodes especially in the axilla. (Other presentations are discussed later under Clinical Staging and the Discussion.)

Malignant breast disease in the Western hemisphere affects women predominantly greater than 45 years and a smaller number is seen below 35 years^{2,5,10}. The disease in younger patients is thought to be more aggressive though some disagree⁵. This appears to be similar to the picture seen in Africa except that in the west only 2 % of patients are younger than 35 years compared to the disease in Africa where the majority women are younger than 35 years ^{6,7,11,19}.

STAGING OF BREAST DISEASE

Staging refers to the grouping of patients according to the extent of their disease. Staging of breast cancer is performed clinically initially and is aimed at judging a patient's post treatment prognosis^{11,35}. This is based on clinical findings alone, although this may be assisted by radiological and other pre-operative investigations. Findings obtained at operation or by histological examination are not included.

Unfortunately, experience has shown that patients do not pass from one stage to the next as disease progresses although any method of staging suggests that this should be the case. In addition to the unpredictable nature of the disease, lymph nodes may enlarge because of hyperplasia rather than tumour involvement and the presence of lymph nodes may be disputable even between experienced hands. Further more, it is now accepted that another explanation for the enlargement is a host reaction in the form of hyperplasia in regional lymph nodes³⁵.

The most widely used system for staging primary breast cancer is that proposed by the

International Union Against Cancer (UICC) and the American Joint Committee on Cancer (AJCC). The UICC classification is the most commonly used and has incorporated the Tumour Node Metastasis (TNM) classification in its most recent usage³⁵. Another important staging system is the Manchester classification and is not mentioned here.

TNM CLASSIFICATION

Based on the description of the primary tumour (T), the status of regional lymph nodes (N), and the presence of distant metastasis (M). Reports may contain numerical codes behind each letter, such as $T_2N_1M_0$ referring to a tumour greater than 2cm but less than 5 cm (T_2), the presence of palpable nodes on the homolateral axillary nodes (N_1), and the absence of distance metastasis (M_0). This would give a stage II cancer under the UICC classification.

UICC CLASSIFICATION³⁶

Stage 0 - $T_{is} N_0 M_0$, Carcinoma in situ

Stage I - $T_1 N_0 M_0$,

Stage IIA - $T_0 N_1 M_0$, $T_1 N_1 M_0$, $T_2 N_0 M_0$

Stage IIB - $T_2 N_1 M_0$, $T_3 N_0 M_0$

Stage IIIA- $T_0 N_2 M_0$, $T_1 N_2 M_0$, $T_2 N_2 M_0$, $T_3 N_{1,2} M_0$, $T_4 N_{any} M_0$

Stage IIIB- $T_4 N_{any} M_0$, $T_{any} N_3 M_0$

Stage IV - $T_{any} N_{any} M_0$

Where for

T_1 tumour ≤ 2 cm in greatest diameter

T_2 tumour >2 cm to 5cm

T_3 tumour >5 cm

T_4 tumour of any size has invaded chest wall and/or skin

N_0 no regional lymph node metastasis

N_1 metastasis to movable ipsilateral axillary node(s)

N_2 metastasis to ipsilateral axillary node(s) fixed to one another or to other structures

N_3 metastasis to ipsilateral internal mammary lymph node(s)

M_0 no distant metastasis

M_1 distant metastasis

TREATMENT

In stages I and II (UICC Classification) complete removal of breast tissue - total mastectomy- is advisable in the majority of patients, together with axillary exploration. Axillary dissection may involve simple excision of a pectoral node for histological examination or complete clearance of the axillary contents in the form of a modified radical mastectomy. Sentinel node identification and dissection can be carried out in advanced local disease^{35,37}.

In stage III disease, total mastectomy is advised, provided that this will result in complete removal of the breast tumour (and involved underlying muscles) and allow for adequate skin closure³⁵. This is usually followed up with chemotherapy, radiotherapy and hormonal therapy. Pre-operative tumour reduction with these treatment modalities has been advocated.

In stage IV disease, treatment involves no more than palliation. Mastectomy may be advised in order to deal with or to prevent fungation. Radiotherapy and Chemotherapy may also be used as adjuvant treatment in all cases of tumour treatment.

OBJECTIVE OF THE STUDY

Main objectives of the study was to determine:-

- (a) The frequency of known risk factors associated with breast cancer in Zambian women attending the University Teaching Hospital.
- (b) The presentation of breast cancer in patients seen at the University Teaching Hospital.

Secondary Objectives were:-

- (a) To determine possible aetiological factors of breast cancer in patients attending the University Teaching Hospital.
- (b) To determine stage at presentation
- (c) To recommend appropriate interventions in dealing with the problem of breast cancer in Zambia

METHODOLOGY

This was a prospective uncontrolled observational study in patients with breast cancer attending the University Teaching Hospital. Patients were interviewed and information recorded in a Performa (see appendices).

Clinical examination and results of necessary laboratory tests conducted were entered in the same Performa.

Study population:-

Thirty-seven patients attending the tumour clinic and the general surgical units at the University Teaching Hospital were interviewed and examined. These patients were either being seen for the first time or were already being attended to by one of the general surgical units. As such some patients were seen and interviewed from the tumour clinic while with others this was done by the bed side in the wards they were being admitted. Histology results were sought postoperatively for the patients undergoing biopsies and definitive operations. These were reviewed in collaboration with the histopathology laboratory staff. The usual care for patients with breast cancer was taken in all cases.

The collected data was entered into a performa and later analysed using simple descriptive methods.

Time frame:-

The study spanned an 8 month period beginning February 2003.

Inclusion criteria:-

All patients with clinical and histopathologically determined breast cancer were included in the study and informed consent was obtained from each patient.

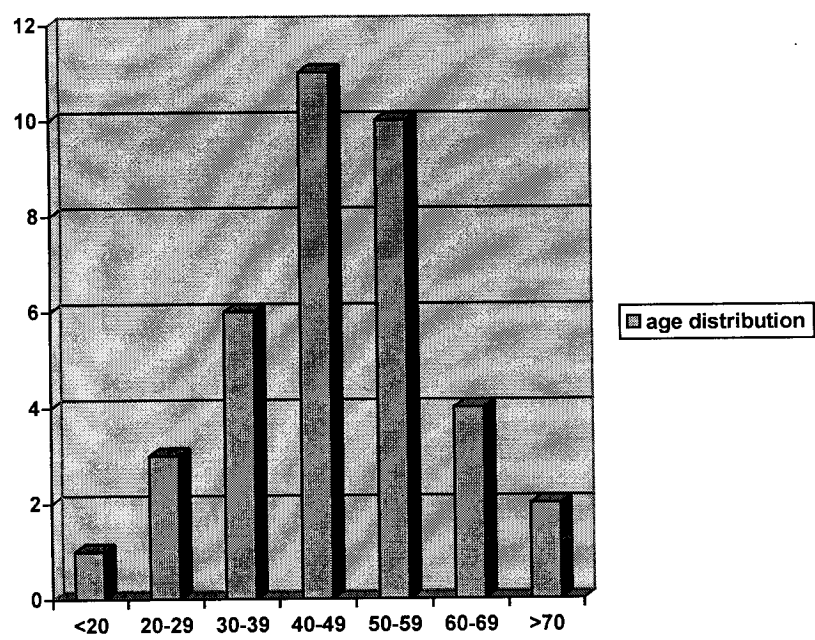
Ethical Consideration: -

Permission had been sought prior to commencing the study from the Ethics Committee of the University of Zambia regarding the study involving human subjects. Similarly, consultants in charge of the various surgical units at the University Teaching Hospital gave permission to study their patients.

RESULTS

Thirty-seven women with breast cancer were interviewed and their ages ranged from 18 to 71. All patients reported on their own. Their mean age 48.6 years.

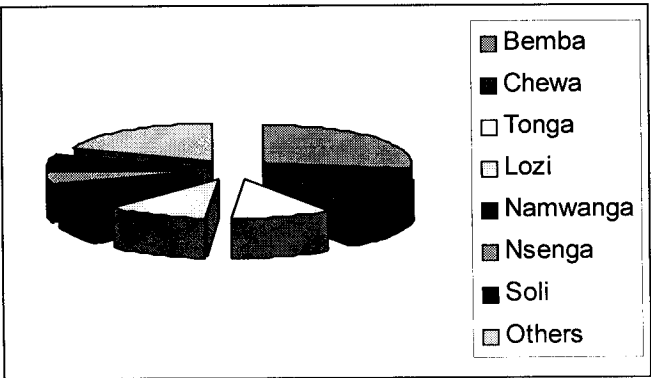
FIG1



Twenty-one (56.8%) of the women were less than 50 years of age and the majority of them were in the age group 40-49. Below is their age frequency distribution. Two of the women had bilateral carcinoma, one patient being premenopausal.

Fig 1

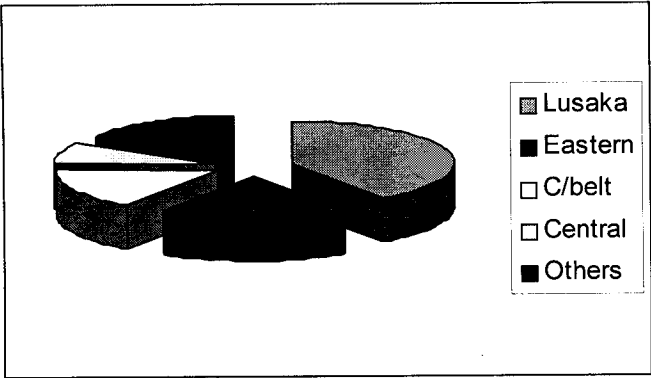
Tribes of affected patients(n=37)



Predominantly they were of the Bemba tribe of the Northern province and residing in Lusaka province. *As can be noted some tribes were represented by only one patients.

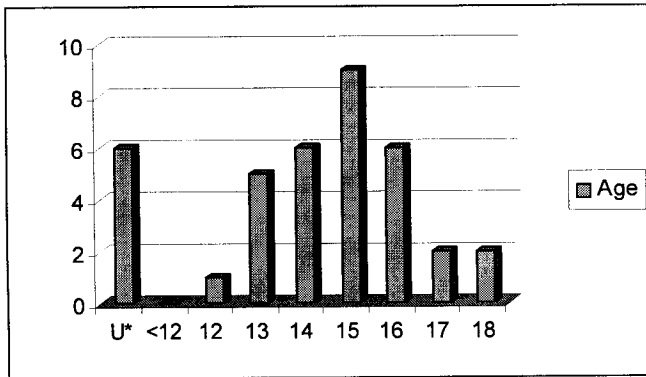
Fig 2

Patients residence(n=37)



The majority of patients were residing in Lusaka and Eastern province at the time of diagnosis.

Table3
Age at menarche(n=37)



U* = unknown

Table 1
Reproductive lifespan of post menopausal women (n=11)*

												Average
age at menarche	14	15	15	15	16	16	16	17	17	18	14	16
age at menopause	47	41	48	53	39	42	48	44	51	47	52	46.3
length of reproductive life	33	26	33	28	23	26	32	27	34	29	34	30

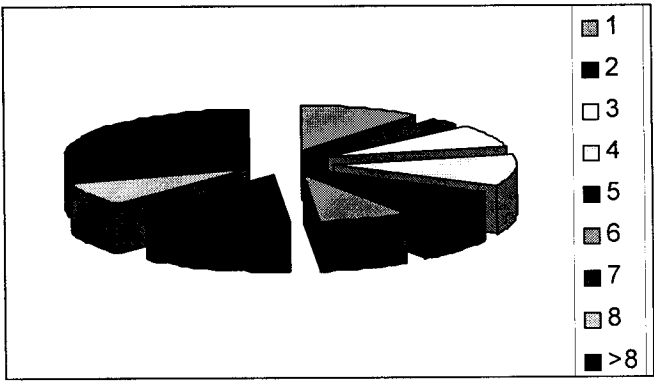
*Full details known only for 11 patients, rest of patients could not recollect.

The category of post menopausal women was 18 (48.6%). The reproductive life span of the women was from 23 to 34 years, averaging 30.0 years.

Mean age at menopause was 46.3. years

Mean age at menarche=14.9years

Table 5
Parity(n=37)



Four patients had only one child, all others had two or more children.

Table 2
Age at first pregnancy*(n=32)

age	15	16	17	18	19	20	21	22	23	24	25	26	27
no.patients	3	3	5	6	5	3	2	3	0	1	0	0	1

*5 patients could not recollect event

As can be noted most patients had their first child below the age of 22 and only two had children after that age with 5 patients unable to recollect the year of the event.

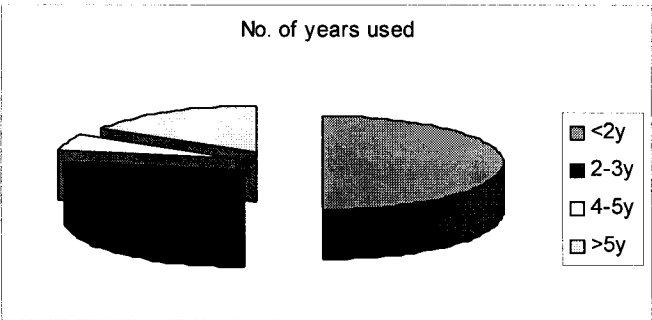
Table 3
Breastfeeding habits(n=37)

	Premenopausal patients	Postmenopausal patients
Never breastfed	1	0
Breastfed	18	18

Mean cumulative breastfeeding time was sixty months for this group of patients. (This was calculated by finding the cumulative breastfeeding period for each woman and getting the mean for the whole group).

Contraceptive use:

Fig 6
Contraceptive use(n=18)



Of those who had used contraceptives, 18(48.6%),only 7 were using them at the time of diagnosis or had used them in the ten years prior to onset of symptoms.

Table 9
Income bracket of patients(n=37)

<i>Income bracket</i>	<i>No. of patients</i>
Low<K250,000	24
Medium K250-K500,000	10
High>K500,000	3

Most patients were of a low-income category, 24(64%).

Fig7
Income bracket of patients

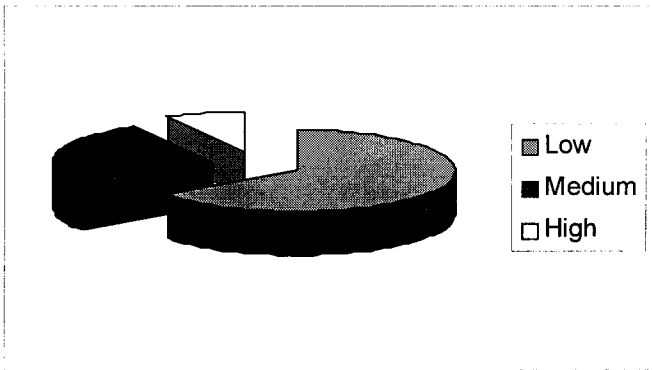
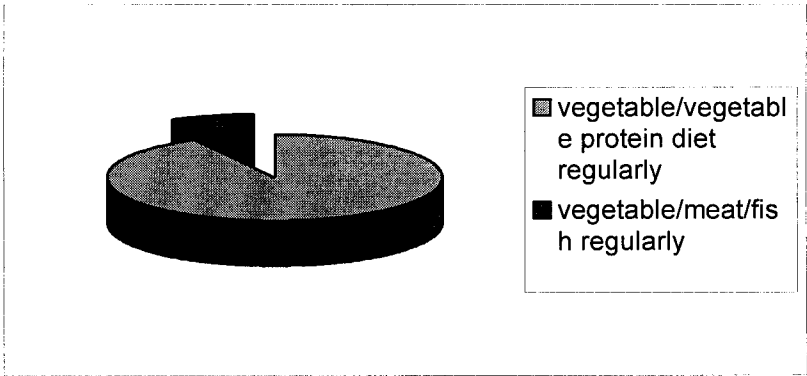


Table5
Body Mass Index(n=37)

<i>BMI</i>	<i>WHO Classification</i>	<i>Frequency</i>
>18.5	Under weight	9
18.5 - 24.9	Normal weight	13
25.0 - 29.9	Over weight grade1	10
30.0 - 39.9	Over weight grade2	5
40.0 or higher	Over weight grade3	0

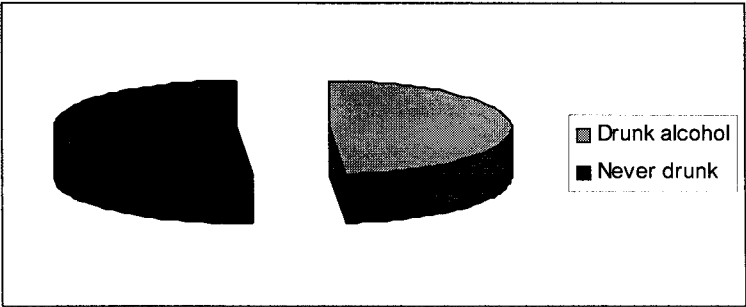
BMI = weight (kg)/square of height (m²), is used as a measure of expected bodyweight for a given height of the body. The patients studied fell within the mildly overweight, normal or under weight categories of the WHO classification.

Fig 8
Predominant diet(n=37)



The women were all having a diet predominantly of vegetable, vegetable based protein and carbohydrates (92.0%) and in only 3 patients was there regular intake of animal and animal fat based foods.

Fig 9
Alcohol intake(n=37)



Of the 37 subjects in the study almost half(18) had taken alcohol prior to the onset of their symptoms but only 4 were heavy drinkers.

Table 6
Alcohol intake(n=18)

Mild alcohol consumption (occasional drinker)	7
Moderate alcohol consumption (regular drinker-occasionally drunk)	7
Heavy drinker (regularly drunk)	4

Smoking habits-

Only three (3) of the thirty-seven patients interviewed had smoked in their lifetime. There is no known information about smoking in the general population.

Family history

Cancer in Sibling	1
Cancer in Mother	1
Cancer in Aunt	2

There were only 4 of the 37 patients interviewed that had a family history known. Of these 3 were postmenopausal and 1 was premenopausal. In one the relative affected was a sibling ,in two an aunt and in the other a mother.

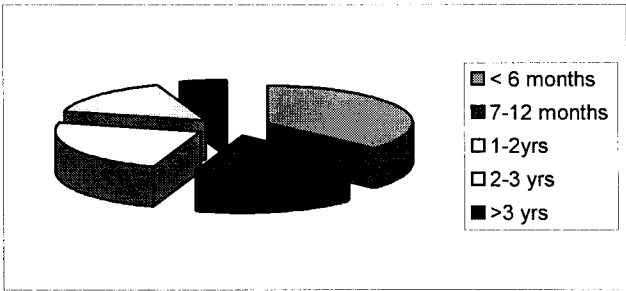
DISEASE CHARACTERISTICS:

Most patients presented to the hospital late, the majority presenting 6 months after noting the first symptom. Two patients had their cancer diagnosed during pregnancy, all in the second trimester. The first symptom of disease in the women was mainly that of a breast lump in 72.5% of patients and this was the main symptom they presented with at the health institution.

Table 7
Duration of complaints before seeking medical attention(n=37).

Time period	No. of patients
<3 months	6
3-6 months	7
7-12 months	7
1-2 years	9
2-3 years	6
>3 years	2
Total	37

Fig 10
Duration of complaints before seeking medical attention



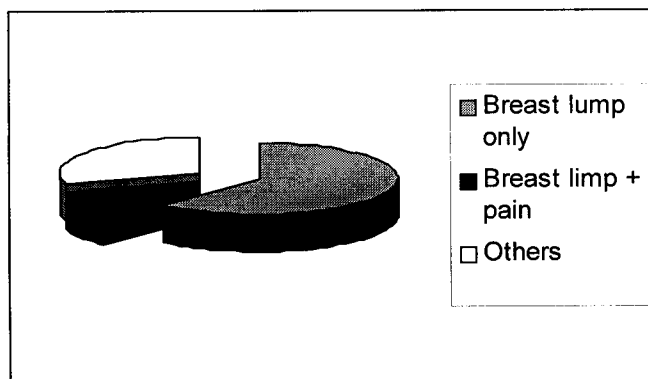
Most patients sought medical attention after six months of noting the problem.

Table 8
First symptoms noticed by patients(n=37)

	<i>Symptoms</i>	<i>Frequency</i>
1	Breast lump	23
2	Pain only	1
3	Axillary lymphnode	2
4	Breast lump + lymphnode	0
5	Breast lump + pain	3
6	Nipple discharge	1
7	Lump + nipple disharge	2
8	Lump + nipple discharge + pain	0
9	Nipple discharge + pain	1
10	Unknown	4
	<i>Total</i>	<i>37</i>

Fig 11

First symptoms noticed by patients



The women's first symptom was mostly of a lump. Pain was not a common initial complaint.

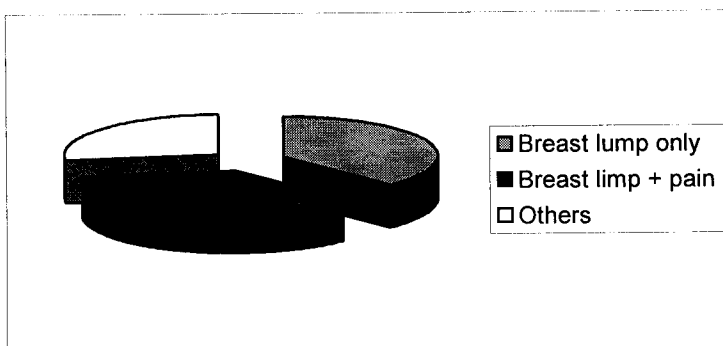
Table 9

Presenting Symptoms(n=37)

	<i>Symptoms</i>	<i>Frequency</i>
1	Breast lump only	14
2	Pain only	0
3	Axillary lymph node only	0
4	Breast lump + lymph node	3
5	Breast lump + pain	13
6	Nipple discharge	3
7	Breast lump + nipple discharge	0
8	Lump + nipple discharge + pain	1
9	Nipple discharge + pain	0
10	Ulceration	3
	Total	37

Fig 12

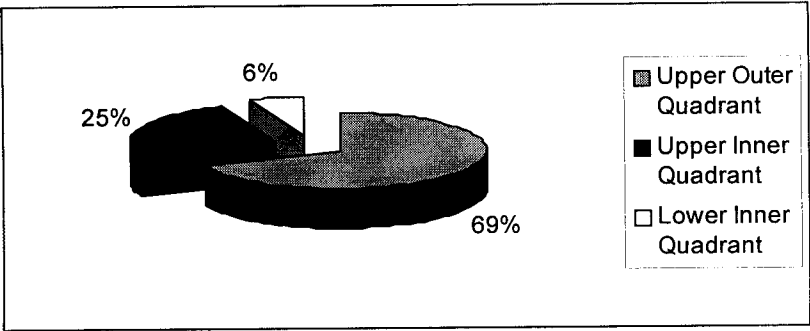
Presenting symptoms



As can be noted most women presented with a lump. The lump was reported to be either painful or painless. Ulceration and nipple discharge were other less common presentations.

Fig 13

Tumour site at presentation(n=37)



State of the tumour at presentation

>5cm(large tumour).....	21 (56.8 %)
Free of pectoralis muscles/fascia.....	19 (51.4 %)
Skin tethering.....	9 (24.3 %)
Peau d' orange.....	9 (24.3 %)
Nipple retraction.....	8 (21.6 %)
Fungating tumour.....	5 (13.5 %)
Nipple discharge.....	3 (8.1 %)
Lymphoedema of arm.....	2 (5.4 %)

Lymph nodes involved

- Axillary in 28 patients (75.6 %)
- Supraclavicular in one (2.7 %)

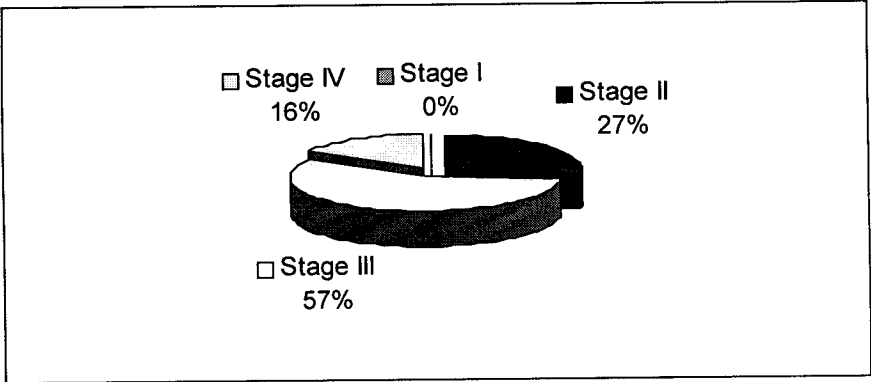
Fifty-six percent of the lesions were large tumours (>5cm at largest diameter) and free of the underlying pectoralis muscles (51.4 %). One had a fungating tumour of the axilla and yet another had no nodal involvement despite having a large fungating tumour.

Clinical stage at presentation(n=37)

Stage I.....	0
Stage II.....	10
Stage III.....	21
Stage IV.....	6

Fig 14

Clinical stage at presentation(n=37)



Histopathology results(n=21)

Infiltrating ductal carcinoma.....15

Infiltrating lobular carcinoma.....1

Adenoid tubular carcinoma.....1

Paget’s disease of the nipple1

Medullary carcinoma.....1

High grade cutaneous Non Hodgkins disease.....1

Moderately to poorly differentiated squamous cell carcinoma.....1

*It was possible to collect only twenty-one histology results because of various logistical problems.

Only six (6) tumours were graded using the Modified Nottingham system: one was a grade I , two were grade II and the rest high grade III tumours. All the grade III cancers were in pre-menopausal women and they had presented within a year of onset of symptoms.

DISCUSSION

Overview of breast cancer:

The breasts are modified sweat glands more fully developed in the female and secrete milk. Each breast is composed of 15 to 20 lobes of compound alveolar glands that radiate out from the nipple. They are in clusters of ‘bunches of grapes’ with lactiferous ducts that carry milk from the glands to the nipple¹. Breast cancer originates in the lactiferous duct epithelial lining or the breast stroma².

The commonest type of malignant breast tumour seen in Zambia is infiltrating ductal carcinoma⁴. This is similar to the picture seen elsewhere^{5,7,14}. The term *ductal carcinoma* refers to its origin from the ductal epithelium².

Malignant breast tumours under the WHO classification are as follows³⁷:

1 Non infiltrating (intraductal and intralobular carcinoma)

2 Infiltrating carcinoma

infiltrating ductal

medullary

tubular

mucinous

infiltrating lobular

Paget's disease of the nipple

The primary site of breast cancer involvement is the upper outer quadrant, principally on the right. This is probably attributable to the increased amount of breast tissue at that site¹⁰. Spread of breast cancer is by direct infiltration into the breast parenchyma along mammary ducts, and through the breast lymphatics¹⁰.

Commonest lymph nodes involved are axillary, internal mammary and supraclavicular

nodes respectively. About 40 % of patients have axillary node involvement and the likelihood of axillary nodal involvement appears to be related to the size of the primary tumour. The combination of the presence and extent of metastases to the axilla represents the single most important prognostic factor for patients with breast cancer^{10,35,38,39}. The second major site of regional nodal metastases for carcinoma of the breast are the internal mammary lymph node chain that lies at the anterior ends of the intercostal spaces alongside the internal thoracic vessels¹⁰.

Early diagnosis confers a better prognosis in breast cancer^{2,5,10}. This has been well documented and one of the prognostic factors is the level of tumor spread at presentation. This will affect the treatment modalities used^{10,35}.

Clinical breast examination (CBE) by physicians and breast self examination (BSE) by the patient is considered the most important way to detect breast cancer early. Various other methods are known but the most commonly used are mammography, a modified roentgenogram, and fine needle aspiration cytology^{2,27,39}. Mammography is useful and more accurate in postmenopausal patients and could be of use in Zambia.

Fine needle aspiration biopsy (FNAB) of the lumps found on mammography or clinically is used to ascertain the preliminary histological diagnosis⁵. Most surgeons though would not base their final decision solely on cytology. One study in Zambia showed that predictive breast lump aspiration could be useful in assisting surgeons make early diagnosis of breast disease⁴¹.

Thus fine needle aspiration Biopsy (FNAB), mammography and clinical evaluation are currently the mainstay of diagnosis in many centres. These could be of use here in Zambia.

DISCUSSION OF RESULTS

Thirty-seven patients were interviewed and examined. The risk factors common to breast cancer were studied in this group of afflicted women to ascertain how much of the well-known risk factors are seen in our area.

Age:

They were noted to be of mainly a younger age group than their western counterparts as in most other studies done in the region ^{7,11,19}. (The majority of patients in the study were in the age bracket 40 to 49 years.) The disease as pointed out in literature review affects a much younger age group here in Africa, most studies done putting the figure at a decade earlier than the western breast cancer^{7,14, 15}. It was expected though that a much younger age group would have been affected as series done in the region have shown before⁷. The mean age was 48.8, not very different from a study done in Zambia on the histology of breast cancers seen⁹. .

Tribes of patients:

The patients studied were all Zambian black women and of diverse tribal origins the majority hailing from the Eastern and Northern provinces of the country but residing predominantly in Lusaka. Perhaps the easy accessibility of these provinces to rail and road transport, and thus to the University Teaching Hospital in Lusaka may have to do with these findings. It is also well known that 30% of the Zambian population is of the Bemba ethnic group of the Northern province, followed by the Nyanja of the Eastern province⁴² .

Family history:

There was a family history noted in four (10.8%) of the patients studied. It has been shown in the literature that this is the single most important risk factor for breast cancer^{2,5,10}. This is as in the literature worldwide. Family history is usually associated with cancer in the younger pre-menopausal patients but our patients developed the disease post menopausally. Larger groups of patients would have to be assessed to prove this finding.

Menarche/Menopause:

The patients were equally distributed (i.e, post menopausal 50%) and had not had an early age at menarche less than 12 years in all the cases. Most studies show a higher proportion of post menopausal women. There is, in the general Zambia population, a larger number of pre menopausal women than was noted in this study though⁴².

As noted earlier in the literature, early menarche and late menopause which increase the length of the reproductive life have been shown to considerably increase the risk for breast cancer development^{2,10}. Ssali et. al. in their series of 86 patients also noted this to be the case¹⁹. In their series they found that the patients with breast cancer actually had a higher age at menarche than their control patients.

In this study group, of the postmenopausal patients, only one had a late menopause, later than 55 years. All the post menopausal patients had a short menstrual life which does not concur with the information noted in the literature worldwide^{24,30}.

Contraceptive use:

Almost half of the patients used contraceptives but only for a short duration. In a few patients contraceptives had been used at some stage ten years prior to the onset of symptoms. There is an increased risk of developing breast cancer with contraceptive use up to ten years after stopping them^{24,30}. In the general population only 17% of women use contraceptive methods and of these only 9% use hormonal contraception⁴². This suggests that there was a significantly increased use of contraceptives among the patients studied.

Parity:

The average number of children born to a Zambian woman in her reproductive life is 5 and she would have had her first child by age eighteen⁴¹. Of the patients studied none was

nulliparous and four (10.8%) only had one child each. Majority of patients had more than four children (78.1%). In the literature it is thought that a younger age at first term pregnancy confers a protective effect against breast cancer development^{2,10}. Their mean age at first pregnancy was 17.3% and the majority had their first children before twenty-two years of age. Two (5.4%) had their cancer diagnosed in the second trimester of pregnancy.

In this study, it would appear that age at first pregnancy and parity did not seem to have a major protective effect in the causation of breast cancers in the women as other series have shown^{2,10,19}.

Lactation:

The patients studied had a mean cumulative breastfeeding period of 60 months. This figure is higher than what is given for most series that have shown the protective effect of lactation against breast cancer development^{19,22}. In this group of patients studied it appears this was not a contributory factor in protection against breast cancer development. Ninety percent of Zambian children are breastfed and weaning occurs between 6 months of age and 34 months of age⁴². Perhaps with the breast carcinoma we encounter here in Zambia and the sub region there could be other factors that are responsible for protection against its causation.

Socio-economic status:

The socio-economic status of the study group did not differ significantly with that of the general population⁴². As with other series done in the region most patients were of the low-income bracket¹⁹. The large series done by Sharp et.al. showed that patients from deprived backgrounds have larger tumours at operation and higher grade tumours³⁴. This can probably explain why people from poorer areas, such as in the majority of black Africa, have poorer outcomes and why despite having the majority of protective characteristics our women are still at risk. And yet the specific factors responsible for increasing the risk within our environment need to be investigated more fully.

Diet:

From the study it would appear that the patients studied were on a regular basis eating vegetable-based foods. Few of the patients were eating animal based proteins and fats and so few patients were exposed to the high fat diets associated with a higher risk for cancer^{4,34}. These findings are similar to those found by others in the region^{7,1,19}. The diet of the study group did not differ significantly with that of the general population⁴².

Body Mass Index:

A look at the BMI's of the patients shows that the majority of patients fell within the normal or underweight range. Others were in the grade 1 overweight group. BMI did not seem to be a factor therefore in these patients. It would have been expected that this group of patients should probably have had higher BMI values than what was noted. Higher BMI values and hence worse WORLD HEALTH ORGANIZATION (WHO) grading have been implicated in the aetiology of cancers and it is thought that the risk is greater in the Caucasian population³⁴. Intake of high fibre diet has also been shown to have a protective effect against the development of breast cancer³ but as can be noted our patients have a higher fibre intake. A study quoted earlier showed though that a higher starch intake could be associated with an increased risk and our women here take a diet high in carbohydrate³³. This could be one of the risk factors here and awaits further scientific investigation.

Alcohol intake:

More than half of the patients drunk alcohol but only 4(10.8%) were heavy drinkers regularly inebriated. From literature it has been noted that increased alcohol intake is associated with a greater risk of developing breast cancer^{24,30}.

Zambian women, according to demographic and health surveys done, are not given to alcohol intake and only 23% are known to have drunk alcohol in their life. Of these less than 30% were moderate to heavy drinkers⁴².

Alcohol use in the women in this study, therefore, would appear to be much higher than in the general population and may be a significant risk factor for breast cancer. However, larger numbers are required to determine statistical significance.

Discussion of presenting symptoms:

Most of the patients who participated in the study discovered the tumour on their own. This is as in the literature^{5, 10,12} and shows the importance of women being aware of signs and symptoms of breast cancer hence the need for better community education.

The bulk of the patients presented late, later than 6 months as noted in other studies done in Africa^{7,11,15,19}. The main presenting symptom was of a lump in the breast with or without pain at the site. The part of the breast most affected was the upper outer quadrant. These findings are consistent with those of other series noted in the literature^{2,5,12}. The cancers studied were predominantly large tumours free of the pectoralis fascia and muscles. There was nodal involvement in 75% of the patients with only one patient having a supraclavicular node. This is as noted elsewhere in the literature^{12,14,19}. The results from the examinations were unremarkable in as far as the known clinical presentation in the literature.

Of the histopathology results collected the majority were 'infiltrating ductal carcinoma' which is well known in the literature⁹ but two biopsy results showed tumours not normally found in the breast. These were 'squamous cell carcinoma' and 'Non-Hogkins lymphoma'. Of the six that had histopathology grade included, half were high-grade tumours. Looking at the characteristics of the clinical tumour presentation it would be expected that most of the tumours would be high grade, presenting in younger women¹⁴.

CONCLUSION

Breast cancer in *Zambian* women occurs in a relatively younger age group consistent with earlier studies reported in the regional literature. A larger proportion were pre-menopausal than noted in the literature.

The pattern of breast cancer presentation is similar to that seen in other series done in the region and is of a *mass* discovered by the patient. This *mass* could be painful or painless and there is associated axillary lymphadenopathy in the majority of cases.

Risk factors noted in this study that could be contributory to the development of breast cancer included a higher contraceptive use than the rest of the population and an increased alcohol consumption. Low socio-economic status, parity, breastfeeding and a short reproductive life did not seem to confer protection to this group of women.

Studies with larger numbers of subjects would be necessary to substantiate these findings in the aetiology of breast cancer in *Zambia*.

RECOMMENDATIONS

1. The majority of patients discover the lump on their own hence breast self examination (BSE) needs to be promoted in the community. Clinical breast examination (CBE) needs to be introduced as part of maternal and child health care clinics as well. This will inevitably reduce the time from discovery of the tumour to presentation at the health care provider. As a consequence the overall picture of morbidity and mortality is likely to improve.
2. There is also the need for better breast cancer awareness among the health care personnel who work at various maternal and child health care facilities to help them make a timely and appropriate referral.
3. There is need for a large study to assess the risk and aetiological factors in our environment.
4. These results can be used as the basis for more detailed epidemiological studies on breast cancer in Zambia.

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APPENDICES

STUDY PROTOCOL

All patients in the study shall give informed consent

All patients shall be interviewed and their responses entered in a questionnaire.

Clinical examination of all patients shall be done including a full breast examination.

This shall be conducted in the relevant clinical examination rooms in the wards. The patient's privacy will be maintained. Patients already operated on shall have their clinical presentation prior to surgery noted in the form to be used.

Tissue diagnosis will be obtained in the patients

Data analysis of study material shall then be carried out.

PATIENT'S INFORMATION SHEET

(Handed to the patient)

The study to be undertaken shall be used to assess the frequency of known risk factors for breast cancer in Zambia. It shall be conducted at the University Teaching Hospital and other centres where permission will be granted.

Upon giving consent and being included in the study the patient will be interviewed and examined. A biopsy, where a piece of breast tissue is excised and taken to the laboratory to determine the nature of disease, shall be done.

The various treatments and investigations shall not in anyway disturb the patient's treatment

INFORMED CONSENT FORM

Title: Malignant breast disease at the University Teaching Hospital – frequency of known risk factors and presentation.

Introduction:

My name is Dr. Bruce Bvulani, a registrar in the department of surgery in the University Teaching Hospital. I am conducting a research, which is looking into factors responsible for causing breast cancer in the University Teaching Hospital.

Before you can decide to volunteer for the study you will be given a chance to see what your participation entails and its possible implications. If you do consent to participate in the study we may carry out a biopsy, which means to get a piece from the breast for laboratory tests to confirm the presence of breast cancer. While doing this you will experience some pain and there may be some bleeding from the wound. During this time all the necessary care and treatment will be given to you for the healing process.

Risks and benefits:

By participating in the study there will be no risk except the pain after an operation for which necessary care will be given while you are in hospital.

There is no direct financial benefit or gain by participating in the study and by participating in this study you will receive an early diagnosis, advice and appropriate treatment from the researcher and other medical personnel. Should you develop any complication or injury during your participation in the study you will be provided with the standard care available at the hospital.

Voluntary participation:

Giving consent to participate in this study does not mean violation of your rights. If you wish to withdraw at any time or seek clarification you may do so. This will not affect the standard of care you will otherwise receive even if you were not in the study. Your participation is purely voluntary.

Confidentiality:

All necessary information obtained in the study will be kept confidential. Care will be taken to maintain privacy throughout your participation in the study.

Acceptability to participate:

By now I am sure you have understood the nature of this study and its implications. If you wish to participate in the study, please put your thumbprint or signature on the space provided.

If you wish to seek clarification please contact:

Dr Bruce Bvulani, PO BOX 33704, Lusaka, Tel 096-782098,Lusaka

.....

Patient's thumbprint or signature

.....

Witness' signature

.....

Researcher's signature

CLINICAL ASSESSMENT

General examination:

WtHt..... (BMI=)

Breast examination: (diagram)

Contour
Presence of lump, fungation (etc).....
Presence of peau d' orange.....
Size of lump (cm).....
Attached or mobile.....
Skin Tethering.....
Nipple retraction.....
Nipple discharge.....

Lymph nodes involved/state of nodes:

Axillary:
Other nodes: -.....
Final UICC Clinical stage.....